

### **REMARKS**

Claims 17-19 are pending in the application. Claims 17-19 have been amended to delete the terms “, and only the CpG dinucleotide,” and “endogenous mammalian chromosomal DNA”. No new matter has been added. Each presently maintained rejection is addressed below.

#### **Written description (new matter)**

Claims 17-19 are rejected as containing new matter for the inclusion of the term “, and only the CpG dinucleotide,”. Claims 17-19 have been amended to delete this term. Applicants respectfully submit that this amendment overcomes this rejection and respectfully request that this rejection be withdrawn.

#### **Obviousness**

Claims 17-19 are rejected as being obvious over the combination of Matulic-Adamic et al., Zhang et al., and Tamsamani et al. (“the primary references”) in view of Bennett et al. (“Bennett”). The primary references are relied upon for the proposition that it would have been prima facie obvious at the time of the invention to one of ordinary skill in the art to chemically modify (including a 2'-O-methyl modification) the 5' or 3' terminal ribose of any known oligonucleotide therapeutic to improve the stability of the oligonucleotide against exonuclease degradation. Indeed, this is the problem that the primary references were intended to solve.

Bennett is relied upon for teaching antisense oligonucleotides targeting VCAM-1, an endogenous mammalian chromosomal DNA. Fortuitously, Bennett's SEQ ID NO:63 has a single CpG dinucleotide at its 3' end.

Thus, the rejection maintains that it would have been obvious in view of the primary references to modify the 3' terminal CpG of Bennett's SEQ ID NO:63 to make that oligonucleotide more stable against exonuclease degradation.

Applicants sought to solve a different problem. Applicants were the first to discover that 2'-O-methylation of a CpG dinucleotide reduces the unwanted side effects of splenomegaly and depletion of platelets caused by the presence of the CpG dinucleotide in an oligonucleotide. As neither the primary references, nor Bennett sought to address this problem, it is purely fortuitous that Bennett provides an oligonucleotide that happens to have a 3' terminal CpG that might have been obvious to modify to improve oligonucleotide stability.

Claims 17-19 have been amended to remove the term “endogenous mammalian chromosomal DNA”, thereby eliminating Bennett’s SEQ ID NO:63 as prior art against amended claims 17-19. Applicants respectfully submit that this amendment overcomes the rejection and request that the rejection be withdrawn.

Applicants acknowledge that they had elected “endogenous mammalian chromosomal DNA”, with traverse, as a species election for initial examination. However, Applicants respectfully request further examination of the amended claims, now drawn to oligonucleotides that are complementary to a genomic region or gene, or to RNA transcribed from such a gene, wherein such gene or RNA transcript is from a eukaryotic or prokaryotic pathogen, or a virus selected from the group consisting of human immunodeficiency virus (type 1 or 2), influenza virus, herpes simplex virus (type 1 or 2), Epstein-Barr virus, cytomegalovirus, respiratory syncytial virus, hepatitis B virus and hepatitis C virus.

Applicants seek favorable consideration of this request for the following reasons. Applicants discovery that 2'-O-methylation of a CpG dinucleotide reduces the unwanted side effects of splenomegaly and depletion of platelets caused by the presence of the CpG dinucleotide in an oligonucleotide was an important discovery that was completely nonobvious in view of the primary references. This should not be diminished by the fact that Bennett fortuitously provided an oligonucleotide that could be modified for entirely different reasons. In addition, the amendment was necessitated by the newly applied new matter rejection. Finally, Applicants believe that the scope of the amended claims has already been searched during prosecution of this application.

### **CONCLUSION**

In view of the above remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner believes that any discussion of this communication would be helpful, the Examiner is invited to call the undersigned attorney at 207-571-9365, x-107.

Respectfully submitted,

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